10/591482 IAP9 Rec'd PCT/PTO 01 SEP 2006

## SEQUENCE LISTING

:110> Bayerische Julius-Maximilians-Universität Würzburg :120> Mutein of a bone morphogenetic protein and use thereof :130> S 10019 PCT <160> 33 <170> PatentIn version 3.1 <210> 1 <211> 114 <212> PRT <213> Homo sapiens <220> <221> MISC FEATURE <222> (1)..(114) <223> BMP-2 <400> 1 Gln Ala Lys His Lys Gln Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr Asn His Ala Ile Val Gln 55 Thr Leu Val Asn Ser Val Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu 90 Lys Val Val Leu Lys Asn Tyr Gln Asp Met Val Val Glu Gly Cys Gly 100 105 Cys Arg <210> 2

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Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp 20 25 30

Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr Cys His Gly Asp 35 40 45

Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr Asn His Ala Ile 50 55 60

Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile Pro Lys Ala Cys 65 70 75 80

Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu 85 90 95

Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met Val Val Glu Gly 100 105 110

Cys Gly Cys Arg 115

PCT/EP2005/002328 WO 2005/085281

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Lys	His	Glu 35	Leu	Tyr	Val	Ser	Phe 40	Arg	qaA	Leu	Gly	Trp 45	Gln	Asp	Trp	
Ile	Ile 50	Ala	Pro	Glu	Gly	Tyr 55	Ala	Ala	Phe	Tyr	Суз 60	Asp	Gly	Glu	Cys	
Ser 55	Phe	Pro	Leu	Asn	Ala 70	His	Met	Asn	Ala	Thr 75	Asn	His	Ala	Ile	Val 80	
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Ser Ser Ala Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg 20

Lys His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp 40 45

Gln Thr Leu Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys 85 90 95

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105 110

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Cys Gly Cys His

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caagacctgg gatggcagga ctggatcatt gcacccaagg gctatgctgc caattactgt 180
gatggagaat gctccttccc actcaacgca cacatgaatg caaccaacca cgcgattgtg 240
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Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn 70

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro

Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 105

Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr 120

Arg Asn Met Val Val Arg Ala Cys Gly Cys His 135

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Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro 85 90 95

Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr
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Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

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aaggcgtgct gtgcacccac caagctgagc gccacctctg tgctctacta tgacagcagc 360
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Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys
35 40 45

Glu Gly Leu Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn 50 55 60

His Ala Val Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr 65 70 75 80

Pro Pro Thr Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu 85 90 95

Phe Ile Asp Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met
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Val Val Glu Ser Cys Gly Cys Arg 115 120

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ccaccc	acct 9	gctgt	gtgc	c ca	cgcg	gctg	agt	ccca	tca	gcat	cctc	tt c	attg	actct	
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Pro P	ro Ser	Cys	Cys 85	Val	Pro	Thr	Lys	Leu 90	Thr	Pro	Ile	Ser	Ile 95	Leu	
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Ala Pro Leu Asp Tyr Glu Ala Tyr His Cys Glu Gly Val Cys Asp Phe

75

70

65

Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Ile Ile Gln Thr 90 Leu Leu Asn Ser Met Ala Pro Asp Ala Ala Pro Ala Ser Cys Cys Val 110 100 Pro Ala Arg Leu Ser Pro Ile Ser Ile Leu Tyr Ile Asp Ala Ala Asn 120 125 115 Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu Ala Cys Gly 135 Cys Arg 145 <210> 18 <211> 438 <212> DNA <213> Mus musculus <220> <221> misc\_feature <222> (1)..(438) <223> GDF-7 <400> 18 actgcgctgg ctgggactcg gggagcgcag ggaagcggtg gtggcggcgg tggcggtggc 60 ggcggcggcg gcggcggcgg cggcggcggc ggcggcag gcaggggcca cgggcgcaga 120 ggccggagcc gctgcagtcg caagtcactg cacgtggact ttaaggagct gggctgggac 180 gactggatca tcgcgccatt agactacgag gcataccact gcgagggcgt ttgcgacttt 240 cctctgcgct cgcacctgga gcctaccaac cacgccatca ttcagacgct gctcaactcc 300 atggcgcccg acgctgcgcc agcctcctgc tgcgtgcccg caaggctcag tcccatcagc 360 attetetaca tegatgeege caacaaegtg gtetacaage agtacgaaga catggtggtg 420 438 gaggcctgcg gctgcagg <210> 19 <211> 108 <212> PRT <213> Homo sapiens

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12/21

12/21
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Lys Glu Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Pro Gly Tyr Glu 20 25 30
Ala Tyr Glu Cys Arg Gly Val Cys Asn Tyr Pro Leu Ala Glu His Leu 35 40 45
Thr Pro Thr Lys His Ala Ile Ile Gln Ala Leu Val His Leu Lys Asn 50 55 60
Ser Gln Lys Ala Ser Lys Ala Cys Cys Val Pro Thr Lys Leu Glu Pro 65 70 75 80
Ile Ser Ile Leu Tyr Leu Asp Lys Gly Val Val Thr Tyr Lys Phe Lys 85 90 95
Tyr Glu Gly Met Ala Val Ser Glu Cys Gly Cys Arg 100 105
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Phe Glu Asp Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Lys Glu Tyr 20 25 30

Glu Ala Tyr Glu Cys Lys Gly Gly Cys Phe Phe Pro Leu Ala Asp Asp 35 40 45

Val Thr Pro Thr Lys His Ala Ile Val Gln Thr Leu Val His Leu Lys 50 55 60

Phe Pro Thr Lys Val Gly Lys Ala Cys Cys Val Pro Thr Lys Leu Ser 65 70 75 80

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Tyr His Tyr Glu Gly Met Ser Val Ala Glu Cys Gly Cys Arg 100 105 110

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His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile 25

Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro 40

Phe Pro Pro Ala Asp His Leu Asn Ser Thr Asn His Ala Ile Val Gln

Thr Leu Val Asn Ser Val Asn Ser Lys Ile Pro Lys Ala Cys Cys Val

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Lys Val Val Leu Lys Asn Tyr Gln Asp Met Val Val Glu Gly Cys Gly 105 100

Cys Arg

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Cys Pro Phe Pro Pro Ala Asp His Leu Asn Ser Thr Asn His Ala Ile 55

Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile Pro Lys Ala Cys 75 70

Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu 90

Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met Val Val Glu Gly 105

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Ser Ser Val Gly Asp Tyr Asn Thr Ser Glu Gln Lys Gln Ala Cys Lys

Lys His Glu Leu Tyr Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp

Ile Ile Ala Pro Glu Gly Tyr Ala Ala Phe Tyr Cys Asp Gly Glu Cys 55

Ser Phe Pro Pro Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val 65 70

Gln Thr Leu Val His Leu Met Phe Pro Asp His Val Pro Lys Pro Cys

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 105

Ser Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ser 120

PCT/EP2005/002328 WO 2005/085281

Cys Gly Cys His 130

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Ser Ser Ala Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg

Lys His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp 40 35

Ile Ile Ala Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly Glu Cys

Ser Phe Pro Pro Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val

Gln Thr Leu Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys 90

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105

Asn Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala 115 120

Cys Gly Cys His 130

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Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg 35 40 45

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala 50 55

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Pro Asn Ser Tyr Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro 85 90 95

Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 100 105 110

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Arg Asn Met Val Val Arg Ala Cys Gly Cys His 130 135

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Pro Gln Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser 20 25 30

His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln

45

18/21

40

Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Pro Asp Ser Cys Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro 85 90 95

Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr 100 105 110

Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

Arg Asn Met Val Val Lys Ala Cys Gly Cys His 130 135

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Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys 35 40 45

Glu Gly Leu Cys Glu Phe Pro Pro Arg Ser His Leu Glu Pro Thr Asn 50 60

His Ala Val Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr 65 70 75 80

Pro Pro Thr Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu 85 90 95

Phe Ile Asp Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met 100 105

Val Val Glu Ser Cys Gly Cys Arg 115 120

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<211> 120

<212> PRT

<213> Mus musculus

<220>

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<222> (1)..(120)

<223> GDF-6 mutein

<400> 30

Thr Ala Phe Ala Ser Arg His Gly Lys Arg His Gly Lys Lys Ser Arg

Leu Arg Cys Ser Arg Lys Pro Leu His Val Asn Phe Lys Glu Leu Gly 25

Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Tyr His Cys

Glu Gly Val Cys Asp Phe Pro Pro Arg Ser His Leu Glu Pro Thr Asn

His Ala Ile Ile Gln Thr Leu Met Asn Ser Met Asp Pro Gly Ser Thr

Pro Pro Ser Cys Cys Val Pro Thr Lys Leu Thr Pro Ile Ser Ile Leu 85 90

Tyr Ile Asp Ala Gly Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met 100 105 110

Val Val Glu Ser Cys Gly Cys Arg 120

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<211> 146

<212> PRT

<213> Mus musculus

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<222> (1)..(146)

<223> GDF-7 mutein

<400> 31

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25

Ala Gly Arg Gly His Gly Arg Arg Gly Arg Ser Arg Cys Ser Arg Lys 40

Ser Leu His Val Asp Phe Lys Glu Leu Gly Trp Asp Asp Trp Ile Ile

Ala Pro Leu Asp Tyr Glu Ala Tyr His Cys Glu Gly Val Cys Asp Phe 70

Pro Pro Arg Ser His Leu Glu Pro Thr Asn His Ala Ile Ile Gln Thr

Leu Leu Asn Ser Met Ala Pro Asp Ala Ala Pro Ala Ser Cys Cys Val 105

Pro Ala Arg Leu Ser Pro Ile Ser Ile Leu Tyr Ile Asp Ala Ala Asn 115 120

Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu Ala Cys Gly 130 135

Cys Arg 145

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<211> 108 <212> PRT

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<400> 32

Asn Ala Lys Gly Asn Tyr Cys Lys Arg Thr Pro Leu Tyr Ile Asp Phe

Lys Glu Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Pro Gly Tyr Glu 25

Ala Tyr Glu Cys Arg Gly Val Cys Asn Tyr Pro Pro Ala Glu His Leu

Thr Pro Thr Lys His Ala Ile Ile Gln Ala Leu Val His Leu Lys Asn 55

Ser Gln Lys Ala Ser Lys Ala Cys Cys Val Pro Thr Lys Leu Glu Pro

Ile Ser Ile Leu Tyr Leu Asp Lys Gly Val Val Thr Tyr Lys Phe Lys

Tyr Glu Gly Met Ala Val Ser Glu Cys Gly Cys Arg 100 105

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<211> 110

<212> PRT

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<400> 33

Ser Ala Gly Ala Gly Ser His Cys Gln Lys Thr Ser Leu Arg Val Asn 10

Phe Glu Asp Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Lys Glu Tyr

Glu Ala Tyr Glu Cys Lys Gly Gly Cys Phe Phe Pro Pro Ala Asp Asp

Val Thr Pro Thr Lys His Ala Ile Val Gln Thr Leu Val His Leu Lys , . 55

Phe Pro Thr Lys Val Gly Lys Ala Cys Cys Val Pro Thr Lys Leu Ser

Pro Ile Ser Val Leu Tyr Lys Asp Met Gly Val Pro Thr Leu Lys 85

Tyr His Tyr Glu Gly Met Ser Val Ala Glu Cys Gly Cys Arg 105